holocarboxylase synthetase deficiency

Holocarboxylase synthetase deficiency is an inherited disorder in which the body is unable to use the vitamin biotin effectively. This disorder is classified as a multiple carboxylase deficiency, a group of disorders characterized by impaired activity of certain enzymes that depend on biotin.

The signs and symptoms of holocarboxylase synthetase deficiency typically appear within the first few months of life, but the age of onset varies. Affected infants often have difficulty feeding, breathing problems, a skin rash, hair loss (alopecia), and a lack of energy (lethargy). Immediate treatment and lifelong management with biotin supplements may prevent many of these complications. If left untreated, the disorder can lead to delayed development, seizures, and coma. These medical problems may be life-threatening in some cases.

Frequency

The exact incidence of this condition is unknown, but it is estimated to affect 1 in 87,000 people.

Genetic Changes

Mutations in the *HLCS* gene cause holocarboxylase synthetase deficiency.

The *HLCS* gene provides instructions for making an enzyme called holocarboxylase synthetase. This enzyme is important for the effective use of biotin, a B vitamin found in foods such as liver, egg yolks, and milk. Holocarboxylase synthetase attaches biotin to certain enzymes that are essential for the normal production and breakdown of proteins, fats, and carbohydrates in the body. Mutations in the *HLCS* gene reduce the enzyme's ability to attach biotin to these enzymes, preventing them from processing nutrients properly and disrupting many cellular functions. These defects lead to the serious medical problems associated with holocarboxylase synthetase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Early-Onset Biotin-Responsive Multiple Carboxylase Deficiency
- Early-Onset Combined Carboxylase Deficiency
- HLCS deficiency
- Infantile Multiple Carboxylase Deficiency
- Multiple Carboxylase Deficiency, Neonatal Form

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C5-OH Acylcarnitine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5-OH.pdf

Genetic Testing

- Genetic Testing Registry: Holocarboxylase synthetase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268581/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/holocarboxylase-synthetase-deficiency
- MedlinePlus Encyclopedia: Pantothenic Acid and Biotin
  https://medlineplus.gov/ency/article/002410.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Pantothenic Acid and Biotin
  https://medlineplus.gov/ency/article/002410.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Holocarboxylase synthetase deficiency
  https://rarediseases.info.nih.gov/diseases/2721/holocarboxylase-synthetase-deficiency

Educational Resources

- Disease InfoSearch: Holocarboxylase synthetase deficiency
  http://www.diseaseinfosearch.org/Holocarboxylase+synthetase+deficiency/3450
- MalaCards: holocarboxylase synthetase deficiency
  http://www.malacards.org/card/holocarboxylase_synthetase_deficiency
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Holocarboxylase%20synthetase%20deficiency&type=profile
- Orphanet: Multiple carboxylase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=148
- Screening, Technology, and Research in Genetics
  http://www.newbornscreening.info/Parents/organicaciddisorders/HCSD.html
- Virginia Department of Health
  http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_MCD_English.pdf

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- Organic Acidemia Association
  http://www.oaanews.org/mcd.html
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/metaboli.html

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22holocarboxylase+synthetase+deficiency%22+OR+%22Multiple+Carboxylase+Deficiency%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28holocarboxylase+synthetase+deficiency%5BTIAB%5D%29+OR+%28biotin-responsive+multiple+carboxylase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- HOLOCARBOXYLASE SYNTHETASE DEFICIENCY
  http://omim.org/entry/253270

Sources for This Summary

- Morrone A, Malvagia S, Donati MA, Funghini S, Ciani F, Pela I, Boneh A, Peters H, Pasquini E, Zammarchi E. Clinical findings and biochemical and molecular analysis of four patients with holocarboxylase synthetase deficiency. Am J Med Genet. 2002 Jul 22;111(1):10-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12124727
- Tang NL, Hui J, Yong CK, Wong LT, Applegarth DA, Vallance HD, Law LK, Fung SL, Mak TW, Sung YM, Cheung KL, Fok TF. A genomic approach to mutation analysis of holocarboxylase synthetase gene in three Chinese patients with late-onset holocarboxylase synthetase deficiency. Clin Biochem. 2003 Mar;36(2):145-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12633764

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